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Translation #1056

ELECTRONIC CHEMISTRY. - Correlation between K^+ and Na^+ in the cycle of polarization renewal of the cellular membrane. Note of Madame Andree Goudot, presented by M. Louis de Broglie.
Compt. Rend. 254:2342-2344, 1962.

Introduction. - The phenomena of nervous conduction and muscular contraction are accompanied by cycles of chemical reactions activated by metal cations. The correlation between cations explains the physiological phenomenon. Thus, the nervous conduction shows itself by a depolarization which spreads on the surface of the nerve membrane. But that depolarization is accompanied by an egress of K^+ and acetylcholine (Ach) connected with an ingress of Na^+, which causes a reversal of the potential of the membrane. Then the reaction is reversed and the positive polarization of the membrane is reestablished.

A theoretical study (1) of the action of Na^+ and K^+ on Ach has shown that in the presence of a phosphoryled component such as carbonyl phosphate, K^+ activates the synthesis of Ach while Na^+ causes dissociation. But that fact is not sufficient to show the role of correlated ion transports.

The morphological study of the membrane shows that it is constituted by molecules of phospholipidae directed parallel to each other. Since the physiological phenomenon occurs on the level with those molecules, it seems evident that it is connected with a cycle of chemical reactions where those molecules intervene. It is a type of reactions belong' ~) dynamic cycles defined by J. Polonovski (2). Hokin and Hokin already had suggested that the "sodium pump" could be explained by the cycle of phosphatidic acids (2). In the case of the nerve: K^+, Ach and Na^+ intervene and their transportation must be considered in the cycle of chemical reactions with the phospholipides of the membrane. Choline being the base of lecithin, one cannot imagine that this cycle would be that of the renewal of the base in lecithin at the same time as that of an acylation. Hence, the use of Ach. This hypothesis has led me to undertake a theoretical study, from the standpoint of electronic chemistry, of the complexes lecithin-K^+ and lecithin-Na^+. Then of the complexes formed by those cations and the dissociated products: Ach, glyceride, PO_4H_2.

K^+ and NA^+ coordination complexes 4 and it can be considered that, given the molecular structure of lecithine, the atoms which are involved in the reaction are situated in the same plane.

Calculation of charges. - Only charges on atoms participating in the dynamic cycle are given here.

Lecithine-K^+ complex:

Diglyceride.

CH_3.	O.	CO.	CH_2......	CH_2.
−0,08	−0,55	+0,82	−0,04	+0,93

Phosphate.

OH.	O_{CP}.	P.	O_{PC}.	OH.
−0,14	+0,31	−0,18	+0,22	−0,09

Choline.

CH_3......	CH_2	$N(CH_3)_3$.
−0,03	−0,14	+0,34

According to the distribution of charges, a break can be foreseen:

1° Between CO (+ 0.82) and CH_2 (-0.04) neutral, thus dissociating an acetyl grouping in the diglyceride.

2° Between CH_2(+0.93) of the diglyceride and Ocp (+0.31) of the phosphate to which it is connected.

3° The connection between Opc (+0.22) of the phosphate and CH_2(+ 0.03) neutral from choline must be rather weak.

On the other hand one can imagine a possible connection between O (-0.55) of the dissociated acetyl grouping and neutral CH_2 of choline.

Lecithine-Na^+ Complex. - The distribution of charges differs little from that of the potassic complex, except that the dissociation of an acetyl grouping in diglyceride is less probable for one has CH_2(-0.14).

Ach-P-Na^+-diglyceride remnant complex. - The calculation of charge distribution was carried out after dissociation of the groupings which had labile connections between them. Phosphate was dissociated from diglyceride and the latter lost an acetyl which formed some Ach with choline. This shows the possibilities of the lecithin synthesis reaction from its elements.

Acétyl-choline.

CH_3.	CO.	O.	CH_2.......	CH_2.	$N(CH_3)_3$.
−0,10	−0,16	+0,27	0,0	−0,14	+0,41

Digiyceride remnant.

CH_2.......	CH_2.
+0,76	+0,96

Phosphate.

OH.	O_{CP}.	P.	O_{PC}.	CH.
+0,03	−0,93	+0,81	−0,94	+0,03

1° A rupture (break) is possible between O(+0.27) and CH_2 neutral of Ach.

2° A connection may occur between CO (-0.16) and CH_2(+0.76), thus resynthetizing the glyceride.

3° The renewal of choline can occur through the intermediary of a phosphate grouping: connection between CH_2(+0.96) and O_{cp}(-0.93), on the one hand and between O_{pc}(-0.94) and CH_2 neutral after dissociation from Ach, on the other hand.

The same reaction cannot be achieved by K^+ which inhibits the dissociation of Ach. It can only be achieved through the intervention of Na^+.

Resonance energies and action potential. - For an identical bioactivator cation, the difference between the energies of resonance of an activated complex and of the complex containing the reaction products yields the activation potential. If that energy is positive, the reaction is spontaneous; if it is negative, that energy must be provided for the reaction to take place. For the potassic complex the activation potential is -20kc. It is therefore necessary to provide an energy of about 20 kc for the reaction with K^+ alone. For the sodium complex the activation potential is -22.19 kc.

The excess of energy provided by the formation of the sodium complex on the energy required for the dissociation of the potassium complex (that is for the depolarization) must represent the action potential. This calculated action potential is about 95 mV, therefore it is very near the experimental value (100 mV).

Note. - The highest occupied orbital in the lecithin-M^+ complex is represented by 2.477Δ, whether it be K^+ or Na^+.

Discussion. - It is therefore possible to imagine a very simplified scheme of the renewal of the membrane potential in the nervous conduction, connected to the dynamic cycle of choline renewal at the same time as that of acetylation in lecithin. That rapid cycle is connected with the formation of Ach and its dissociation, whence the need for correlated action of $K^{(+)}$ and Na^+. The departure of K^{+} and of Ach renders possible the entry of $Na^{(+)}$. Then, according to the cation exchange theory, $K^{(+)}$ comes to take the place of $Na^{(+)}$ in the membrane. Non myelinized nerves are involved in this study.

This scheme seems in agreement with the fact that the K^+/Na^+ exchanges are in a relation equal to I. Furthermore, those exchanges occur very near the outer face of the membrane, as that has been shown, for by injecting cations in axone, they very rapidly move away towards the membrane (A. L. Hodkin). To this rapid cycle must be added a slow cycle where cellular respiratory elements intervene, hence formation of ATP.

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(1) A. Goudot, Proceedings, 253, 1961, p.120.

(2) J. Polonovski, VI-th Latin biochemical days, Geneva, 25-28 May 1961.